DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

QUIDEL CORPORATION
RONALD LOLLAR
SENIOR DIRECTOR, CLINICAL AND REGULATORY AFFAIRS
2005 EAST STATE STREET
SUITE 100
ATHENS OH 45701

December 10, 2014

Re: K143206
Trade/Device Name: Amplivue Bordetella Assay
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory viral panel multiplex nucleic acid assay
Regulatory Class: II
Product Code: OZZ
Dated: November 6, 2014
Received: November 7, 2014

Dear Dr. Lollar:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Uwe Scherf -S for

Sally Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement on last page.

510(k) Number *(if known)*
k143206

Device Name
Amplivue Bordetella Assay

Indications for Use *(Describe)*
The AmpliVue® Bordetella Assay is an in vitro diagnostic test for the qualitative detection of Bordetella pertussis nucleic acids isolated from nasopharyngeal swab specimens obtained from patients suspected of having respiratory tract infection attributable to Bordetella pertussis.

The AmpliVue® Bordetella Assay utilizes helicase-dependent amplification (HDA) of the insertion sequence IS481 and a self-contained disposable amplification detection device that allows for manual evaluation of assay results. The IS481 sequence can also be found in strains of other organisms (i.e., B. holmesii and B. bronchiseptica). B. holmesii infection may cause clinical illness similar to B. pertussis, and mixed outbreaks involving both B. pertussis and B. holmesii infection have been reported. Additional testing should be performed if necessary to differentiate B. holmesii and B. pertussis. B. bronchiseptica is a rare cause of infection in humans. When clinical factors suggest that B. pertussis may not be the cause of respiratory infection, other clinically appropriate investigation(s) should be carried out in accordance with published guidelines.

Negative results for the AmpliVue® Bordetella Assay do not preclude B. pertussis infection and positive results do not rule out co-infection with other respiratory pathogens. Results from the AmpliVue® Bordetella Assay should be used in conjunction with information obtained during the patient's clinical evaluation as an aid in diagnosis of Bordetella pertussis infection and should not be used as the sole basis for treatment or other patient management decisions.

The AmpliVue® Bordetella Assay is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

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"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

510(k) Summary

Applicant:

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Date of preparation of 510(k) summary:

November 05, 2014

A. 510(k) Number:

k143206

B. Purpose for Submission:

To obtain substantial equivalence for the AmpliVue® Bordetella Assay

C. Measurand:

Insertion sequence IS481 of *Bordetella pertussis*

D. Type of Test:

Helicase-dependent amplification (HDA)

510(k) Summary

E. Applicant:

Quidel Corporation

F. Proprietary and Established Names:

AmpliVue® Bordetella Assay

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
OZZ – Bordetella pertussis DNA assay system	Class 2	21 CFR 866.3980 – Respiratory viral panel multiplex nucleic acid assay	Microbiology (83)

H. Intended Use:

1. Intended Use(s):

The AmpliVue® Bordetella Assay is an in vitro diagnostic test for the qualitative detection of *Bordetella pertussis* nucleic acids isolated from nasopharyngeal swab specimens obtained from patients suspected of having respiratory tract infection attributable to *Bordetella pertussis*.

The AmpliVue® Bordetella Assay utilizes helicase-dependent amplification (HDA) of the insertion sequence IS481 and a self-contained disposable amplification detection device that allows for manual evaluation of assay results. The IS481 sequence can also be found in strains of other organisms (i.e., *B. holmesii* and *B. bronchiseptica*). *B. holmesii* infection may cause clinical illness similar to *B. pertussis,* and mixed outbreaks involving both *B. pertussis and B. holmesii* infection have been reported. Additional testing should be performed if necessary to differentiate *B. holmesii and B. pertussis. B. bronchiseptica* is a rare cause of infection in humans. When clinical factors suggest that *B. pertussis* may not be the cause of respiratory infection, other clinically appropriate investigation(s) should be carried out in accordance with published guidelines.

510(k) Summary

Negative results for the AmpliVue® Bordetella Assay do not preclude *B. pertussis* infection and positive results do not rule out co-infection with other respiratory pathogens. Results from the AmpliVue® Bordetella Assay should be used in conjunction with information obtained during the patient's clinical evaluation as an aid in diagnosis of *Bordetella pertussis* infection and should not be used as the sole basis for treatment or other patient management decisions.

The AmpliVue® Bordetella Assay is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.

2. Indication(s) for Use:

   Same as Intended Use.

3. Special conditions for use statement(s):

   - For *in vitro* diagnostic use only
   - For prescription use only

4. Special instrument requirements:

   None

I. Device Description:

The AmpliVue® Bordetella Assay combines simple sample processing, an isothermal amplification technology named helicase-dependent amplification (HDA), and a self-contained disposable amplicon detection device, for the detection of *Bordetella pertussis* from nasopharyngeal swabs.

Patient samples are collected using a nasopharyngeal swab and placed into a liquid medium. Fifty microliters (50 µL) of the sample are then transferred to a process buffer that is provided with the kit and mixed. The Process Buffer tubes are heated at 95 °C for 10 minutes. Fifty microliters (50 µL) of the Process Buffer containing sample is added to a reaction tube containing lyophilized mix of HDA reagents. Included in the reaction mix are the isothermal polymerase, helicase and single stranded binding protein. After completion of the HDA reaction the reaction tube is transferred to the amplicon cartridge containing the running buffer. The amplicon cartridge is closed and inserted into the detection chamber. The detection chamber is activated by depressing the detection chamber

handle. Upon activation, the reservoir containing the running buffer and the 0.2 mL tube containing the amplicon is punctured and the solutions are wicked to the lateral flow strip.

Materials Provided:

- 16 Tests per Kit

Symbol	Component	Quantity	Storage
1	Detection Cassettes	16/kit	2° to 30°C
2	Process Buffer	16 tubes/kit 1.45mL	2° to 30°C
3	Reaction Tubes	16 tubes/kit	2° to 8°C
4	Amplicon Cartridge	16/kit	2° to 30°C

Materials required but not provided:

- External controls for *Bordetella pertussis* (e.g. Quidel Molecular Bordetella Control Set #M117, which contains positive and negative controls, serves as an external processing and extraction control)
- Sterile DNAse-free filter-blocked or positive displacement micropipettor tips
- Micropipettor
- Stopwatch or timer
- Scissors or a blade
- Micro tube tray
- Heat block capable of 95° C ± 2° C temperature
- Heat block with heated lid capable of 64° ± 2° C temperature
- Thermometer

J. Substantial Equivalence Information:

1. Predicate device name(s):

   illumigene® Pertussis DNA Amplification Assay

2. Predicate 510(k) number(s):
   K133673

510(k) Summary

3. Comparison with predicate:

Similarities		
Item	**AmpliVue® Bordetella Assay**	**illumigene® Pertussis DNA Amplification Assay (k133673)**
Intended Use	The AmpliVue® Bordetella Assay is an in vitro diagnostic test for the qualitative detection of *Bordetella pertussis* nucleic acids isolated from nasopharyngeal swab specimens obtained from patients suspected of having respiratory tract infection attributable to *Bordetella pertussis*. The AmpliVue® Bordetella Assay utilizes helicase-dependent amplification (HDA) of the insertion sequence IS481 and a self-contained disposable amplification detection device that allows for manual evaluation of assay results. The IS481 sequence can also be found in strains of other organisms (i.e., *B. holmesii* and *B. bronchiseptica*). *B. holmesii* infection may cause clinical illness similar to *B. pertussis,* and mixed outbreaks involving both *B. pertussis and B. holmesii* infection have been reported. Additional testing should be performed if necessary to differentiate *B. holmesii and B. pertussis. B. bronchiseptica* is a rare cause of infection in humans. When clinical factors suggest that *B. pertussis* may	The *illumigene*® Pertussis DNA Amplification Assay, performed on the *illumipro-10™,* is a qualitative in vitro diagnostic test for the direct detection of *Bordetella pertussis* in human nasopharyngeal swab samples taken from patients suspected of having respiratory tract infection attributable to *Bordetella pertussis.* The *illumigene* Pertussis assay utilizes loop-mediated isothermal DNA amplification (LAMP) technology to detect *Bordetella pertussis* by targeting the IS481 insertional element of the *Bordetella pertussis* genome. The IS481 insertional element can also be found in *Bordetella holmesii* and

510(k) Summary

Similarities		
Item	**AmpliVue® Bordetella Assay**	**illumigene® Pertussis DNA Amplification Assay (k133673)**
	not be the cause of respiratory infection, other clinically appropriate investigation(s) should be carried out in accordance with published guidelines. Negative results for the AmpliVue® Bordetella Assay do not preclude *B. pertussis* infection and positive results do not rule out co-infection with other respiratory pathogens. Results from the AmpliVue® Bordetella Assay should be used in conjunction with information obtained during the patient's clinical evaluation as an aid in diagnosis of *Bordetella pertussis* infection and should not be used as the sole basis for treatment or other patient management decisions.	*Bordetella bronchiseptica* strains. Respiratory infection with *Bordetella pertussis, Bordetella holmesii* or *Bordetella bronchiseptica* may yield positive test results in IS481 assays. *B. holmesii* infection may cause clinical illness similar to *B. pertussis,* and mixed outbreaks involving both *B. pertussis* and *B. holmesii* infection have been reported. Additional testing should be performed if necessary to differentiate *B. holmesii* and *B. pertussis. B. bronchiseptica* is a rare cause of infection in humans. When clinical factors suggest that *B. pertussis* may not be the cause of respiratory infection, other clinically appropriate investigation(s) should

510(k) Summary

Similarities		
Item	**AmpliVue® Bordetella Assay**	**illumigene® Pertussis DNA Amplification Assay (k133673)**
		be carried out in accordance with published guidelines. Negative results for the *illumigene* Pertussis DNA Amplification Assay do not preclude *Bordetella pertussis* infection and positive results do not rule out co-infection with other respiratory pathogens. Results from the *illumigene* Pertussis assay should be used in conjunction with information obtained during the patient's clinical evaluation as an aid in diagnosis of *Bordetella pertussis* infection and should not be used as the sole basis for treatment or other patient management decisions. *illumigene* Pertussis is intended for use in hospital, reference or

510(k) Summary

Similarities		
Item	**AmpliVue® Bordetella Assay**	**illumigene® Pertussis DNA Amplification Assay (k133673)**
		state laboratory settings. The device is not intended for point-of-care use.
Sample Types	Nasopharyngeal swab specimens obtained from patients suspected of having respiratory tract infection attributable to *Bordetella pertussis*	Same
Sample Heat Lysis	Manual	Same
Target Sequence Detected	*Bordetella pertussis* IS481 insertional element	Same

Differences		
Item	**AmpliVue® Bordetella Assay**	**illumigene® Pertussis DNA Amplification Assay (k133673)**
DNA Amplification Technology	Helicase-dependent amplification (HDA); self-contained	Loop-Mediated Isothermal Amplification (LAMP); self-contained and automated
Self-Contained System Assay after sample preparation	No	Yes
Detection Technique	Manual	Automated
Instrument	None	*illumipro-10™*

510(k) Summary

Differences		
Item	**AmpliVue® Bordetella Assay**	**illumigene® Pertussis DNA Amplification Assay (k133673)**
Testing Time	85 - 90 minutes	60 -70 minutes

K. Standard/Guidance Document Referenced (if applicable):

Not applicable

L. Test Principle:

The AmpliVue® Bordetella Assay detects *Bordetella pertussis* DNA isolated from nasopharyngeal swab specimens obtained from symptomatic patients suspected of having respiratory tract infection attributable to *Bordetella pertussis*. The assay consists of three major steps: 1) specimen preparation, 2) isothermal Helicase-Dependent Amplification (HDA) of a target sequence of *B. pertussis*, and 3) detection of the amplified DNA by target-specific hybridization probes via a colorimetric reaction on a lateral-flow strip which is embedded in a self-contained disposable cassette to prevent amplicon contamination.

Patient samples are collected using a nasopharyngeal swab and placed into a liquid medium. Fifty microliters (50 µL) of the sample are then transferred to a process buffer that is provided with the kit and mixed. The Process Buffer tubes are heated at 95 °C for 10 minutes. Fifty microliters (50 µL) of the Process Buffer containing sample is added to a reaction tube containing lyophilized mix of HDA reagents.

A HDA reaction is carried out in the Reaction Tube which contains lyophilized HDA reagents, dNTPs, primers and probes. Incubation at 64°C for 60 minutes results in isothermal amplification of the target sequence by *B. pertussis* specific primers. The amplified DNA is detected by a set of specific detection probes included in the Reaction Tube: *B. pertussis* target hybridizes to two specific probes labeled with Biotin (BioTEG) and 6-carboxyfluorescein (FAM). A competitive process control (PRC) is included in the Lysis Tube to monitor specimen processing and inhibitory substances in clinical samples, reagent failure or device failure. The PRC target is amplified and hybridizes to the PRC specific probes labeled with Biotin (BioTEG) and 2,4-dinitrophenyl (DNP).

Following completion of the HDA reaction, the Reaction Tube is transferred to a proprietary Cassette for detection. The Cassette is comprised of two components: 1) an

510(k) Summary

Amplicon Cartridge that holds the running buffer and the 0.2 mL Reaction Tube and 2) the Detection Chamber which houses the Amplicon Cartridge and an embedded vertical-flow DNA detection strip. The DNA detection strip is coated with anti-FAM and anti-DNP antibodies. Once the Cassette is closed, a razor blade and plastic pin located at the bottom of the Cassette opens the Reaction Tube and running buffer bulb, resulting in the release of their contents. The contents flows through a fiberglass paper connected to the DNA detection strip that is attached to a fiberglass pad pre-loaded with streptavidin-conjugated color particles. The *B. pertussis* amplicon with biotin- and FAM-labeled probes is captured by the anti-FAM antibodies at the test (T2) line, and the Process Control amplicon with biotin- and DNP-labeled probes is captured by the anti-DNP antibodies at the control (C) line. The streptavidin-conjugated color particles bind to the biotin in the probe-amplicon hybrid and the test results are displayed in the Cassette window as colored T2 and/or C lines that are visible to the naked eye.

Detection of *B. pertussis* is reported when the T2 line is visible through the detection window of the Cassette. No detection of *B. pertussis* is reported when only the C line is displayed. The assay is regarded as invalid when none of the lines are displayed.

M. Performance Characteristics:

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility

In order to confirm the reproducibility of the AmpliVue Bordetella Assay a blinded and randomized study panel containing *Bordetella pertussis* (BP) negative and positive samples (5x and 2x,) were tested at three (3) test sites (one in-house laboratory and two (2) clinical sites). Each site tested a reproducibility panel and Assay Controls for five (5) days in triplicate. Testing was done by two operators at each site. Each operator ran the panel once a day using one lot of AmpliVue Bordetella Assay. A total of four hundred fifty (450) specimens were tested (including controls). The AmpliVue Bordetella Assay generated reproducible results in this study.

Category	SITE						Overall Percent Agreement		95% Confidence Interval
	Site #1		Site #2		Site #3				
	#expected results/# tested	*% Agreement*	*#expected results/# tested*	*% Agreement*	*#expected results/# tested*	*% Agreement*			
BP Low Positive	30/30	100%	30/30	100%	30/30	100%	90/90	100%	95.9% to

510(k) Summary

Category	SITE						Overall Percent Agreement		95% Confidence Interval
	Site #1		Site #2		Site #3				
	#expected results/# tested	*% Agreement*	*#expected results/# tested*	*% Agreement*	*#expected results/# tested*	*% Agreement*			
(4,716 cfu/mL)									100%
BP Moderate Positive (11,790 cfu/mL)	30/30	100%	30/30	100%	30/30	100%	90/90	100%	95.9% to 100%
BP Negative	30/30	100%	30/30	100%	30/30	100%	90/90	100%	95.9% to 100%
BP Positive Control	30/30	100%	30/30	100%	30/30	100%	90/90	100%	95.9% to 100%
BP Negative Control	30/30	100%	30/30	100%	30/30	100%	90/90	100%	95.9% to 100%

The results suggest that there are no significant differences between different users and different sites on different days. Reproducibility studies are acceptable.

b. Linearity/assay reportable range:

Not applicable – This assay is qualitative.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Traceability:

Not applicable. This assay is qualitative.

Specimen Stability:

A study was performed to determine the specimen stability using a contrived sample at 2x LOD. The contrived sample was stored at 2°C to 8°C for varying lengths of time (24, 48, 72 and 96-hours). The samples were brought to room temperature and tested with the AmpliVue Bordetella Assay.

Based on this study the contrived 2x LOD sample was stable when stored at 2°C to 8°C

Controls:

Controls (Quidel Molecular Bordetella Control Set #M117, which contains positive and negative controls, serves as an external processing and extraction control) were run on the AmpliVue® Bordetella Assay each day of testing. These controls are described as follows:

a. The *process control* is used to monitor sample processing, to detect HDA inhibitory specimens and to confirm the integrity of assay reagents and cassette detection. The process control is included in the Lysis Buffer tube.

b. The *external positive control* may be treated as a patient specimen. The control should be sampled and tested as if it were a swab specimen and processed as described in the Assay Procedure. The external positive control is intended to monitor substantial reagent and cassette failure.

c. The *external negative control* may be treated as a patient specimen. The control should be sampled and tested as if it were a swab specimen and processed as described in the Assay Procedure. The external negative control is used to detect reagent or environmental contamination (or carry-over) by *B. pertussis* DNA or amplicon.

d. Detection limit:

The analytical sensitivity (limit of detection or LoD) of the AmpliVue® Bordetella Assay was determined using quantified (CFU/mL) cultures of two *(2) Bordetella pertussis* bacterial stocks, BP A639 and E431 serially diluted in negative nasal matrix. The LoD is defined as the lowest concentration at which 95% of all replicates tested positive.

The bacterial strains were freshly grown. The cell density of these bacterial suspensions was estimated using the OD_{600} reading. After a cell suspension of 0.25 McFarland units was established, the bacteria were serially diluted in PBS to densities ranging from 3x to 0.3x LoD levels based on preliminary studies.

Each test dilution was run as 20 replicates in the AmpliVue® assay. The highest dilution where at least 19 of 20 replicates show detection of *B. pertussis* (95% positivity) was assigned the Limit of Detection of the strain. The CFU/mL was calculated based on the average bacterial plate count of the dilution.

510(k) Summary

Bacterial Strain	Concentration CFU/mL	Concentration CFU/Assay
A639	2,358	3.93
E431	761	1.27

The assay LOD for *Bordetella pertussis* is 3.93 CFU/assay or 2,358 CFU/mL (sample input).

e. Analytical specificity:

Cross Reactivity:

A study was performed to evaluate the cross-reactivity of the AmpliVue® Bordetella Assay with seventy-nine (79) other microorganisms potentially found in specimens collected to test for *Bordetella pertussis* (BP) infection. Cross-reactive microorganism was tested at clinically relevant levels of viruses (10^5pfu/mL) and bacteria (10^6cfu/mL) in the device. The organisms and their concentrations included in the cross-reactivity study are shown in the table below.

Organism	Test Concentration	
Acinetobacter baumanii	2.90 x10^6	cfu/mL
Arcanobacterium haemolyticum	1.15 x10^6	cfu/mL
Bacteroides fragilis	1.19 x10^6	cfu/mL
Bordetella avium	3.85 x10^6	cfu/mL
Bordetella bronchiseptica	9.45 x10^6	cfu/mL
Bordetella bronchiseptica	1.17 x10^6	cfu/mL
Bordetella bronchiseptica (ATCC 4617)	7.74 x10^6	cfu/mL
Bordetella bronchiseptica	1.97 x10^6	cfu/mL
Bordetella hinzii	1.40 x10^6	cfu/mL
Bordetella holmesii (ZeptoMetrix	3.83 x10^6	cfu/mL
Bordetella holmesii (ATCC 51541)	4.10 x10^6	cfu/mL
Bordetella holmesii (ATCC 700053)	4.70 x10^6	cfu/mL
Bordetella holmesii (ATCC 700052)	4.00 x10^6	cfu/mL
Bordetella parapertussis A747	1.00 x10^6	cfu/mL
Bordetella petrii	6.26 x10^6	cfu/mL
Bordetella trematum	9.24 x10^6	cfu/mL
Burkholderia cenocepacia	2.35 x10^6	cfu/mL
Burkholderia cepacia	2.52 x10^6	cfu/mL
Burkholderia multivorans	1.95 x10^6	cfu/mL
Burkholderia thailandensis	3.95 x10^6	cfu/mL
Chlamydia trachomatis	7.83 x10^6	cfu/mL

510(k) Summary

Organism	Test Concentration	
Chlamydophila pneumoniae	2.10×10^6	DNA copies/mL
Corynebacterium diptheriae	4.00×10^6	cfu/mL
Enterobacter aerogenes	1.31×10^6	cfu/mL
Enterococcus faecalis	3.45×10^6	cfu/mL
Escherichia coli	8.42×10^6	cfu/mL
Fusobacterium necrophorum	3.10×10^6	cfu/mL
Haemophilus influenzae	2.13×10^6	cfu/mL
Klebsiella pneumoniae	1.61×10^6	cfu/mL
Lactobacillus acidophilus	2.00×10^6	cfu/mL
Lactobacillus plantarum	7.97×10^6	cfu/mL
Legionella pneumophilia	1.76×10^6	cfu/mL
Moraxella catarrhalis	9.90×10^6	cfu/mL
Morganella morganii	1.57×10^6	cfu/mL
Mycobacterium avium	1.84×10^6	cfu/mL
Mycobacterium tuberculosis	1.80×10^6	cfu/mL
Mycoplasma pneumoniae	3.16×10^6	cfu/mL
Neisseria gonorrhoeae	2.45×10^6	cfu/mL
Neisseria meningitidis	7.07×10^6	cfu/mL
Neisseria mucosa	1.66×10^6	cfu/mL
Parvimonas micra	1.55×10^6	cfu/mL
Proteus mirabilis	1.06×10^6	cfu/mL
Proteus vulgaris	3.40×10^6	cfu/mL
Pseudomonas aeruginosa	2.60×10^6	cfu/mL
Staphylococcus aureus (MRSA)	7.10×10^6	cfu/mL
Staphylococcus epidermidis	2.14×10^6	cfu/mL
Stenotrophomonas maltophilia	1.90×10^6	cfu/mL
Streptococcus pneumoniae	1.00×10^6	cfu/mL
Streptococcus pyogenes	1.29×10^6	cfu/mL
Streptococcus salivarius	1.70×10^6	cfu/mL
Candida albicans	3.00×10^6	cfu/mL
Adenovirus 31	3.55×10^5	$TCID_{50}$/mL
Adenovirus 31	2.74×10^7	DNA copies/mL
Coronavirus 229E	1.51×10^6	$TCID_{50}$/mL
Coronavirus NL63	1.41×10^5	$TCID_{50}$/mL
Coronavirus OC43	8.51×10^6	$TCID_{50}$/mL
Coxsackievirus B4	1.08×10^5	$TCID_{50}$/mL
Coxsackievirus B5/10/2006	1.02×10^5	$TCID_{50}$/mL
Echovirus 6	1.02×10^6	$TCID_{50}$/mL
Echovirus 7	1.05×10^5	$TCID_{50}$/mL
Echovirus 9	1.41×10^5	$TCID_{50}$/mL

510(k) Summary

Organism	Test Concentration	
Echovirus 11	1.51 x10^6	$TCID_{50}$/mL
Enterovirus 70	1.78 x10^6	$TCID_{50}$/mL
Enterovirus 71	4.17 x10^5	$TCID_{50}$/mL
Epstein-Barr Virus	1.34 x10^6	Virus particles/mL
HSV Type 1 (Mclnytre)	6.65 x10^6	$TCID_{50}$/mL
HSV Type 2 (G)	2.27 x10^6	$TCID_{50}$/mL
Influenza A/Mexico/4108/2009	2.88 x10^6	Virus particles/mL
Influenza B/Florida/04/2006	2.82 x10^6	Virus particles/mL
Measles virus	1.95 x10^6	$TCID_{50}$/mL
Metapneumovirus A1	3.80 x10^6	$TCID_{50}$/mL
Mumps virus	5.89 x10^6	$TCID_{50}$/mL
Parainfluenza Type 1 (#2)	3.97 x10^6	$TCID_{50}$/mL
Parainfluenza Type 2 (Greer)	3.15 x10^6	$TCID_{50}$/mL
Parainfluenza Type 3 (C234)	2.56 x10^6	$TCID_{50}$/mL
Parainfluenza Type 4 (VR-1377)	1.37 x10^6	$TCID_{50}$/mL
Respiratory Syncytial Virus	1.15 x10^6	$TCID_{50}$/mL
Rhinovirus 1A	1.26 x10^6	$TCID_{50}$/mL
Varicella Zoster Virus	1.70 x10^6	DNA copies/mL

The Cross Reactivity study tested a panel of 79 microorganisms. This study determined that 1 of 4 *Bordetella bronchiseptica* strains (strain 4617) and 4 of 4 *Bordetella holmesii* strains tested were cross-reactive with the AmpliVue® Bordetella Assay. These results can be expected as 5% of all *Bordetella bronchiseptica* strains and all *Bordetella holmesii* strains are known to carry the IS481 target sequence. These cross-reactive results are noted in the intended use and limitation sections.

Interference:

A study was conducted to determine if the AmpliVue® Bordetella assay is inhibited in the presence of a panel of seventeen (17) substances potentially present in specimens collected to test for *Bordetella pertussis* infection. Each of the potential interfering substances was tested in three replicates in the presence and absence of near LOD (2x) levels of *B. pertussis* in the AmpliVue® Bordetella Assay. Substances were introduced into the assay at concentrations which were medically relevant.

Common Name	Test Concentration
Cepacol Sore Throat Lozenges	5% w/v
Halls Cherry Menthol-Lyptus Cough Drops	15% w/v
Children's Dimetapp	15% v/v
Chloraseptic Sore Throat Lozenges	10% w/v

510(k) Summary

Ricola Original Swiss Sugar-Free Herb Cough Suppressant Throat Drops	15% w/v
Sucrets Complete Lozenges - Vapor Cherry	5% w/v
Mucin (Bovine Submaxillary Gland, Type I-S)	5 mg/ml
Blood (human), EDTA anticoagulated	5% v/v
Neo-Synephrine	15% v/v
Afrin Nasal Spray Original	15% v/v
Zicam Non-Drowsy Allergy Relief Nasal Gel	5% v/v
Rite Aid Brand Saline Nasal Spray	15% v/v
Zanamivir (Relenza)	5 mg/ml
Tobramycin	4 µg/ml
Mupirocin	10 mg/ml
Oseltamivir Phosphate (Tamiflu)	10 mg/ml
Ricola Original Swiss Sugar Free Herb Cough Suppressant Throat Drops	15% w/v

There was no evidence of interference caused by the substances tested.

Analytical Reactivity (Inclusivity):

The reactivity of the AmpliVue® Bordetella assay was evaluated against an additional six (6) strains of *Bordetella pertussis* at concentrations near the level of detection (LoD) of the assay.

Each strain was tested as three replicates in the AmpliVue® Bordetella. The study was performed in multiple experiments of no more than 14 assays per experiment. For each experiment, three replicates of up to four strains were performed, along with a positive and a negative run control. All seven strains were detected by the AmpliVue® Bordetella Assay.

Bacterial Strain	Concentration CFU/mL	Strain Detected (Yes/No)
9797	2,358	Yes
9340	2,358	Yes
BAA-1335	2,358	Yes
BAA-589	2,358	Yes
51445	2,358	Yes
10380	2,358	Yes

f. Assay cut-off:

Not applicable.

2. Comparison studies:

   a. *Method comparison with predicate device:*

      Not applicable

   b. *Matrix comparison:*

      The compatibility of eight different types of media with the AmpliVue Bordetella assay was determined using Validation Lot reagents and the proposed workflow. Four strains of pre-titered Bordetella pertussis stocks were tested at 1x LoD in the presence of eight different types of media (Tris EDTA, Molecular Grade Water, E-swab, M4, M4-RT, M5, 0.85% Saline).

      For Bordetella pertussis, 4 of 4 strains (A639, E431, BAA 1335, and 51445) were determined to be compatible with the 8 different media types when tested at the assay LoD.

3. Clinical studies:

   a. *Clinical Sensitivity:*

      Performance characteristics of the AmpliVue® Bordetella Assay was established in the Spring to Summer of 2014 (April to August 2014) at four locations in the United States. Eight hundred forty two (842) fresh nasopharyngeal swab specimens were obtained from female and male patients suspected of having respiratory tract infection attributable to *Bordetella pertussis* from were collected and transported to each laboratory for testing with the AmpliVue® Bordetella Assay.

      Clinical performance was based on comparison of the AmpliVue Bordetella Assay results to those obtained by Composite Reference Method that included two manufacturer validated, IS481-targeted real-time PCR assays (PCR1 and PCR2) followed by bi-directional sequencing from PCR positive specimens. The PCR1 and PCR2 assay protocols included 37 amplification cycles. Bi-directional sequencing was performed for all specimens producing amplicon prior to the end of 37-cycle amplification. Specimens were considered positive when bi-directional sequence sequencing results from either comparator PCR assay confirmed the presence of

Bordetella pertussis amplicon. Specimens were considered negative when neither comparator PCR assay produced *Bordetella pertussis* amplicon at the end of the 37-cycles.

Eight hundred forty two (842) fresh nasopharyngeal swab specimens were tested as described above. Six (6) specimens (0.7%) were invalid (in both the initial and repeat test neither the T2 or control lines were detected) and have been removed from additional analysis. The table below details the comparison data of the AmpliVue Bordetella Assay and the Composite Reference Method for the remaining eight hundred thirty six (836) specimens.

Composite Reference Method versus AmpliVue Bordetella Assay			
	Composite Reference Method		
AmpliVue® Bordetella Assay	Positive	Negative	Total
Positive	64	15	79
Negative	2	755	757
Total	66	770	836
			95% CI
Positive Percent Agreement	64/66	97.0%	89.6% to 99.2%
Negative Percent Agreement	755/770	98.1%	96.8% to 98.8%

b. Clinical specificity:

See Section 3a**.**

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off**:**

Not applicable

5. Expected values:

The prevalence of *Bordetella pertussis* detected with the AmpliVue® Bordetella Assay has been calculated for the combined sites based on the age of the patient. Six (6)

specimens (0.7%) were invalid (in both the initial and repeat test neither the T2 or control lines were detected) and have been removed from the Expected Values table. The table below presents the data for the remaining eight hundred forty two (842) specimens.

Combined Study – Expected Values (N=836)			
Bordetella pertussis			
Age	Total #	Total Positive	Prevalence
≤ 2 years	137	8	5.8%
3 to 12 years	274*	27	9.9%
13 to 21 years	145	30	20.7%
≥ 22 years	280**	14	5.0%

* Four (4) specimens were invalid
** Two (2) specimens were invalid

N. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Not applicable.

P. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10, 21 CFR 801.109, and the special controls.

Q. Conclusion:

The AmpliVue® Bordetella Assay is as safe and effective as the predicate device for the qualitative detection of *Bordetella pertussis* nucleic acids isolated from nasopharyngeal swab specimens obtained from patients suspected of having respiratory tract infection attributable to *Bordetella pertussis*.